REMARKS

Claims 1 to 20 were pending in the published PCT application in its published PCT format, including 4 multiple dependent claims. The claims were amended to save fees by eliminating the multiple dependent claims.

The specification was amended to clarify that multidomain polynucleotides of the invention rapidly interconvert from an "off" state to an "on" state, or vice versa, reversibly, on a time scale that is relevant to their use as biosensors and to add the abstract set out on the title page of the published PCT application, WO 00/26226, accompanying this national phase entry.

If the undersigned can advance the prosecution of this application in any way, please call at the number listed below.

Respectfully submitted,

on 2 May 2001 by

MARY M. KRINSKY, Reg. No. 32423
79 Trumbull Street
New Haven, Connecticut 06511-3708
(203) 773-9544

Marked Up Version of Amendments Required by 37 C.F.R. § 1.121

SPECIFICATION, Page 15

As summarized above, polynucleotide sensors of the invention are designed and constructed independently or together to comprise the actuator domain and receptor domain in communication with the bridging domain such that binding of a ligand to the receptor domain and/or a signal triggers a conformational change in the bridging domain which positively and/or negatively modulates the activity of the actuator domain. Where enzyme polynucleotides are employed, the reaction rate may be enhanced or inhibited by reversible binding to small effector molecules such metal ions and/or compounds having a molecular weight of less than about 300. The effector molecule or effect binds to or affects a site that is spatially distinct from that of the enzyme or reporter domain, and rapidly interconvert from an "off" state to an "on" state, or vice versa, or intermediate states between "off" and "on", reversibly,via the bridging domain on a time scale that is relevant for their use as biosensors (*i.e.*, in preferably less than 60 minutes, even more preferably in less than 6 minutes, and in most cases in less than 1 minute, *e.g.*, within seconds). Since they are responsive to ligands and/or signals, multidomain polynucleotides of the invention have a variety of uses, particularly as sensing elements in clinical, industrial, agricultural, and environmental analyses, and as genetic control or report elements for gene expression.

CLAIMS

10 (Amended). A biosensor comprising a polynucleotide according to [claims] claim 1[, 2, 3, 4, 5, 6, 7, 8, or 9].

12 (Amended). A method for detecting the presence or absence of a ligand or its concentration in a sample comprising contacting the sample with a polynucleotide according to [claims] claim 1[, 2, 3, 4, 5, 6, 7, 8, or 9].

19 (Amended). A process for preparing RNA sensors according to [any of claims] claim 15[, 16, 17, or 18].

20 (Amended). A process for preparing DNA sensors according to [any of claims] claim 15[, 16, 17, or 18].